

**REMARKS**

Applicants thank the Examiner for the courtesies extended during the interview conducted at the USPTO on June 5, 2003. As discussed during the interview, claims 66-68, 70-84, and 86-99 are pending and additional claims 100-124 are being added by this Response. In view of the remarks below, withdrawal of the rejections and allowance of the claims are respectfully requested.

Support for claims 100-109 is found in the specification at, for example, page 3, line 35 to page 4, line 5; page 5, lines 11-25; page 7, lines 13-22; page 11, lines 3-10; page 14, lines 7-36; page 17, lines 7-37; Figures 1 and 4; Example 11; and original claims 17-19. See, *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Support for claims 110-124 is found in the specification at, for example, page 3, line 35 to page 4, line 5; page 5, lines 11-25; page 7, lines 13-22; page 11, line 3 to page 12, line 8; page 14, lines 7-36; and page 17, lines 7-37; Figures 1 and 4; Example 11; and original claims 20-34. *Id.*

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments are respectfully solicited.

**Rejection Under § 112, First Paragraph**

Claims 66-68, 70, 72, 73, 79, 80, 82-84, 86, 88, 89, 95, 96, 98, and 99 were rejected under 35 USC §112, first paragraph, for lack of written description. (Paper No. 29 at 2.)

For the reasons set forth below, the rejection is respectfully traversed.

In making the rejection, the Examiner asserted, twice, that "claims that specify the 55kD receptor...would encompass DNA encoding alleles, variants and mutants of said 55kD receptor, wherein the only nucleic acid encoding a 55kD TNF receptor...disclosed in the specification is that of Figure 1." (*Id.* at 2-3, see also, *Id.* at 4.) Based on that repeated assertion, the Examiner contended that rejection of the claims was required in view of the *Lilly* case:

In *University of California v. Eli Lilly and Co.*, 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995), the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id at 1240. In the instant case, the specification has disclosed a single nucleic acid encoding a 55kD TNF receptor with the nucleic acid sequence disclosed in Figure 1. (Paper No. 29 at 3.)

It is respectfully submitted that the facts here are very different from those presented in *Lilly*. In addition, *Lilly* and more recent decisional authority make clear that there is no hard and fast rule that dictates what constitutes a sufficient written description, a fact which the GUIDELINES FOR THE EXAMINATION OF PATENT APPLICATIONS UNDER THE 35 U.S.C. 112 PARA. 1, "WRITTEN DESCRIPTION" REQUIREMENT (MPEP § 2163 (8<sup>th</sup> Ed., Rev. 1, February 2003, pp. 2100-158 to 2100-171)) ("Guidelines") explicitly reflect.

Here, all claims recite DNA encoding a "human" TNF receptor. This alone distinguishes *Lilly*, where the various claims recited DNA encoding "vertebrate," "mammal," "human" and "rat" insulin. Here, unlike in *Lilly*, the specification discloses DNA encoding "human" TNF receptors.<sup>1</sup> Here, the specification describes far more than was described in *Lilly* – and far more than the Patent Office acknowledged in making the final rejection.

DNAs encoding human TNF receptors are described throughout the specification. The Examiner, however, focused only upon the DNAs shown in the Figures. In particular, Figure 1 shows the human "[n]ucleotide and deduced amino acid

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<sup>1</sup> Claims 66 and 67 were amended to recite "human TNF receptor" in our AMENDMENT dated January 14, 2003. Moreover, all of the other claims examined by the Patent Office recited "human tumor necrosis factor binding protein" as originally presented in our AMENDMENT dated August 24, 2000. The Patent Office, however, appears not to have taken this limitation into account in making the present rejection.

sequences for cDNA clone derived from 55 kD TNF-BP. " Page 4, lines 17-18. Figure 4 shows the human "[n]ucleotide sequence and deduced amino acid sequence for cDNA clones derived from 75/65 kD TNF-BP." *Id.*, lines 35-36.

The specification makes plain that the invention possessed by the applicants is *not* limited to the precise sequences mentioned above. Rather, the specification as filed described – and conveyed "possession" of – other sequences, including what the Examiner calls "alleles, variants and mutants." At page 5, lines 11-23, the specification states:

The TNF-binding proteins of the present invention include homogeneous proteins containing the amino acid sequence depicted in Figure 1 or in Figure 4, proteins containing fragments of either sequence, and analogues of any such proteins for example proteins containing amino acid sequences analogous to the sequences of Figure 1 or Figure 4 or to fragments thereof. An analogue is a protein in which one or more amino acids of the sequence depicted in Figure 1 or in Figure 4 have had their side-groups chemically modified in a known manner, or those in which one or more amino acids have been replaced or deleted, without thereby eliminating TNF-binding ability.

The specification as filed expressly described – and conveyed "possession" of – DNA sequences encoding human TNF-binding proteins based on the sequences shown in the Figures, but modified in ways that preserved TNF-binding ability. Specific reference is made to sequences based on "the degeneracy of the genetic code." Page 9, lines 34-37. At page 10, lines 3-10, the specification further states:

That is to say, the present invention embraces not only allelic variants, but also those DNA sequences which result from deletions, substitutions and additions from one or more nucleotides of the sequences given in Figure 1 or Figure 4, whereby in the case of the proteins coded thereby there come into consideration, just as before, TNF-BP. One

sequence which results from such a deletion is described, for example, in Science 248, 1019-1023, (1990).

The specification as filed expressly described – and conveyed “possession” of – DNA subsequences obtainable and based on the starting sequences shown in the Figures. At page 10, lines 12-39, for example, the specification provides:

[T]hose DNA sequences which code for such protein having an apparent molecular weight of about 55 kD, whereby the sequence given in Figure 1 is especially preferred, and sequences which code for non-soluble as well as soluble fragments of such proteins. A DNA sequence which codes, for example, for such a non-soluble protein fragment extends from nucleotide -185 to 1122 of the sequence given in Figure 1. DNA sequences which code for soluble protein fragments are, for example, those which extend from nucleotide -185 to 633 or from nucleotide -14 to 633 of the sequence given in Figure 1. There are also preferred DNA sequences which code for a protein of about 75/65 kD, whereby those which contain the partial cDNA sequences shown in Figure 4 are preferred. Especially preferred DNA sequences in this case are the sequences of the open reading frame of nucleotide 2 to 1,177. The peptides IIA, IIC, IIE, IIF, IIG and IIH are coded by the partial cDNA sequence in Figure 4, whereby the insignificant deviations in the experimentally determined amino acid sequences are based on the cDNA-derived sequence with highest probability from the limited resolution of the gas phase sequencing. DNA sequences which code for insoluble as well as soluble fractions of TNF-binding proteins having an apparent molecular weight of 65 kD/75 kD are also preferred. DNA sequences for such soluble fragments can be determined on the basis of the amino acid sequences derived from the nucleic acid sequences coding for such non-soluble TNF-BP.

Determination of the human TNF receptor amino acid sequences in Figures 1 and 4 is described in Example 7. Page 31, line 24 to page 34, line 10. Determination of DNA sequences encoding the amino acid sequences is described in Example 8. Page 34, line 12 – page 35, line 36. A method for identification and

sequencing of soluble fragments of the amino acid sequences in Figures 1 and 4 is also described. See page 14, lines 7-36:

Starting from the ... amino acid sequences given in Figure 1 as well as in Figure 4 there can be produced, taking into consideration the degeneracy of the genetic code, according to methods known in the art suitable oligonucleotides. By means of these, again according to known methods of molecular biology, cDNA or genomic DNA banks can be searched for clones which contain nucleic acid sequences coding for TNF-BP. Moreover, using the polymerase chain reaction (PCR) cDNA fragments can be cloned by completely degenerating the amino acid sequence of two spaced apart relatively short segments while taking into consideration the genetic code and introducing into their complementarity suitable oligonucleotides as a "primer", whereby the fragment lying between these two sequences can be amplified and identified. The determination of the nucleotide sequences of such a fragment permits an independent determination of the amino acid sequence of the protein fragment for which it codes. The cDNA fragments obtainable by PCR can also, as already described for the oligonucleotides themselves, be used according to known methods to search for clones containing nucleic acid sequences coding for TNF-BP from cDNA or genomic DNA banks. Such nucleic acid sequences can then be sequenced according to known methods. On the basis of the thus-determined sequences and of the already known sequences for certain receptors, those partial sequences which code for soluble TNF-BP fragments can be determined and cut out from the complete sequences using known methods.

Example 9 describes the production of vectors containing DNA encoding a human TNF receptor or the extracellular domain thereof. See page 36, line 32 to page 38, line 7:

For the construction of the expression vector "pN123", this plasmid "pH11" was cleaved the restriction endonuclease Pvull and subsequently treated with alkaline phosphatase. The dephosphorylated vector was thereafter isolated from an agarose gel (V1). The 5'-projecting nucleotides of the EcoRi-cleaved 1.3kb fragment of the 55 kD TNF-BP-cDNA

(see Example 8) were filled in using Klenow enzyme. Subsequently, this fragment was isolated from agarose gel (F1). Thereafter, V1 and F1 were joined together using T4-ligase. *E. coli* HB101 cells were then transformed with this ligation batch according to known methods. By means of restriction analyses and DNA sequencing according to known methods there were identified transformants which had been transformed with a plasmid and which contained the 1.3kb EcoRI fragment of the 55 kD TNF-BP-cDNA in the correct orientation for expression via the HCMV-promotor. This vector received the designation "pN123".

The following procedure was used for the construction of the vector "pK19". A DNA fragment which contained only the cDNA coding for the extracellular part of the 55 kD TNF-BP (amino acids -28 to 182 according to Figure 1) was obtained by PCR technology (Saiki et al., *Science* 230, 1350-1354, 1985, see also Example 8). The following oligonucleotides were used in order to amplify the cDNA from "pN123" coding for the extracellular part of the 55 kD TNF-BP:

BAMHI

5'-CACAGGGATCCATAGCTGTCTGGCATGGGCCTCTCCAC-3'

ASP718

3'-CGTGACTCCTGAGTCCGTGGTGTATTATCTCTAGACCATGGCCC-5'

By means of these oligonucleotides there were also introduced two stop codons of the translation after amino acid 182. The thus-amplified DNA fragment was cleaved with BamHI and Asp718, the thereby resulting projecting ends were filled in using Klenow enzyme and this fragment was subsequently isolated from an agarose gel (F2). F2 was then ligated with V1 and the entire batch was used for the transformation of *E. coli* HB101, as already described. Transformants which had been transformed with a plasmid containing the DNA fragment in the correct orientation for the expression via the HCMV-promoter were identified by DNA sequencing (see above). The plasmid isolated therefrom received the designation "pK19".

*E. coli* strains containing these vectors are described and they have been deposited. See page 17, lines 10-18:

The vectors "pK19" and "pN123" used in Example 9 are especially preferred vectors. These can be isolated according to known methods from *E. coli* strains HB101(pK19) and HB101(pN123) transformed with them. These *E. coli* strains have been deposited on the 26th of January 1990 at the Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under DSM 5761 for HB101(pK19) and DMS 5764 for HB101(pN123)."

The specification also describes human immunoglobulin fragments, their structure and DNA sequences coding for them. Vectors carrying such DNA sequences are described, and have been deposited. See page 17, lines 18-37:

For the expression of proteins which consist of a soluble fragment of non-soluble TNF-BP and an immunoglobulin fragment, i.e. all domains except the first of the constant region of the heavy chain, there are especially suitable pSV2-derived vectors as described, for example, by German, C. in "DNA Cloning" [Vol. II., edt. by Glover, D.M., IRL Press, Oxford, 1985]. The vectors pCD4-H $\mu$  (DSM 5315), pCD4-H $\gamma$ 1 (DSM 5314) and pCD4-H $\gamma$ 3 (DSM 5523) which have been deposited at the Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG, and which are described in detail in European Patent Application No. 90107393.2 are especially preferred vectors. This European Patent Specification and the equivalent Applications referred to in Example 11 also contain data with respect to the further use of these vectors for the expression of chimeric proteins (see also Example 11) and for the construction of vectors for the expression of such chimeric proteins with other immunoglobulin fragments.

Finally, the specification describes the production of chimeric fusion proteins based upon DNA encoding human TNF receptors. See Example 11, page 42, lines 5-28:

Analogously to the procedure in Example 9, the cDNA fragment coding for the extracellular region of the 55 kDa

TNF-BP was amplified in a polymerase chain reaction, but now using the following oligonucleotides as the primer.

Oligonucleotide 1:

Sst I

5'-TAC GAG CTC GGC CAT AGC TGT CTG GCA TG-3'

Oligonucleotide 2:

Sst I

5'-ATA GAG CTC TGT GGT GCC TGA GTC CTC AG-3'

This cDNA fragment was ligated in the pCD4-Hy3 vector [DSM 5523; European Patent Application No. 90107393.2; Japanese Patent Application No. 108967/90; U.S. Patent Application Ser. No. 510773/90] from which the CD4-cDNA had been removed via the SstI restriction cleavage sites. SstI cleavage sites are situated in vector pCD4-Hy3 not only in front of, but also behind the CD4-partial sequence fragment.

In view of the foregoing disclosure, none of which was referenced by the Patent Office in making the rejection, it is submitted that the claimed subject matter is more than adequately described in the specification. As discussed during the interview, neither the PTO's Guidelines nor relevant decisional authority demands more from a specification as filed than is provided here by applicants.

First, adequate written description of claims to genetic material does not require the disclosure of the nucleotide sequence of each species within the scope of the claims. The Guidelines make clear that the written description requirement may be satisfied by just the type of disclosure summarized above.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole.

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An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

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For some biomolecules, examples of identifying characteristics include sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the required possession.

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If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then adequate description requirement is met. Guidelines (MPEP § 2163, pp. 2100-165 to 2100-166.).

DNA sequences encoding human TNF receptors are described in the specification by structure, function and physical properties. Accordingly, the specification contains sufficient disclosure to convey to a skilled artisan that the applicants had possession of the claimed invention. As discussed during the interview, in view of the base sequences that are actually described and the accompanying disclosure of slightly modified molecules based thereon that preserve the described binding property, one skilled in the art would easily and necessarily conclude that applicants were "in possession" of the claimed subject matter. Nothing more is required.

For the Patent Office's convenience of review, copies of the cases discussed at the interview are submitted herewith.

In *Lilly*, the Federal Circuit emphasized that “every species in a genus need not be described in order that a genus meet the written description requirement.” *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997) . In addressing facts that are markedly different from those here, the Federal Circuit stated “[w]e will not speculate on what other ways a broad genus of genetic material may be properly described, but it is clear to us … that the claimed genera of vertebrate and mammal cDNA are not described by the general language of the ‘525 patent’s written description supported only by the specific nucleotide sequence of rat insulin.” *Id.* at 1406. As shown above, the specification here goes far beyond the “general language” and “rat” sequence in *Lilly*.

In post-*Lilly* cases, moreover, the Federal Circuit has repeatedly warned that rigid rules should not be read into the *Lilly* decision.

In *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609, 1615 (Fed. Cir. 2002), the Federal Circuit remanded to the trial court with instructions to consider all relevant evidence bearing on written description. The Court warned that *Lilly* does not hold “that all functional descriptions of genetic material fail to meet the written description requirement.” *Id.* at 1613. The court stated, in particular, “the written description requirement can be met by ‘show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics … i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.’” (*Id.*, citing GUIDELINES FOR EXAMINATION OF PATENT APPLICATIONS UNDER THE 35 U.S.C. 112, ¶ 1 “WRITTEN DESCRIPTION” REQUIREMENT, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001).)

In *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003), the Federal Circuit reiterated that *Lilly* is to be construed in a limited manner:

More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written

description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

In April of this year, after issuance of the final rejection, the Federal Circuit again noted that *Lilly* is restricted largely to its own facts. See *MOBA B.V. v. Diamond Automation Inc.*, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003):

In more recent cases, however, this court has distinguished *Lilly*. For instance, in [*Enzo*], neither the specification nor the deposited biological material recited the precise "structure, formula, chemical name or physical properties" required by *Lilly*. Although this court initially determined that the specification in *Enzo* did not satisfy the *Lilly* disclosure rule, it revisited the issue and remanded to the district court.

The law thus requires only a written description in sufficient detail that one skilled in the relevant art could reasonably conclude that the inventor was in possession of the claimed subject matter. That requirement may be satisfied in any manner, including words, structures, figures, diagrams, examples, sequences, subsequences and/or deposits. All that is required is that the specification convey to one of skill in the art that the applicant was in possession of what is claimed.

It is submitted that applicants' specification as filed did indeed convey to one of skill in the art that the applicants were "in possession" of what is claimed. Reconsideration and withdrawal of the written description rejection are respectfully requested.

### Rejection Under § 103(a)

Claims 66-68, 70, 72, 79, 80, 82, 84, 86, 88, 95, 96, and 98 were rejected under 35 USC §103(a) as being unpatentable over Schall *et al.*, *Cell*, 61:361-70 (1990) ("Schall") in view of Capon *et al.*, U.S. Patent No. 5,428,130 ("Capon"). (Paper No. 29 at 4.)

For the reasons set forth below, the rejection is respectfully traversed.

In making the rejection, the Patent Office asserted that Schall discloses "the nucleic acid sequence encoding an insoluble (eg. membrane bound) TNF receptor (see Figure 1(a), wherein said sequence encodes a receptor that is about 55kD (eg. 415 amino acids, wherein the molecular weight would be 50,578, plus carbohydrate weight because the molecule is glycosylated...))." (*Id.*) The Patent Office further asserted that Schall discloses "the extracellular portion of said molecule." (*Id.*) The Examiner acknowledged, however, that Schall differs from the presently claimed invention in that Schall does not disclose "a nucleic acid encoding an Ig/soluble portion of a 55kD TNF receptor." (*Id.* at 4-5.)

To fill the acknowledged gap, the Patent Office relied upon Capon as disclosing "DNA encoding Ig/ligand binding fusion proteins ... [that] can contain the soluble portion of the cell surface receptor (eg. the receptor minus the transmembrane and cytoplasmic domains...)." (*Id.* at 5.) The Patent Office also asserted that Capon, at "column 10, second paragraph," discloses "the DNA encoding the Ig portion of the fusion protein can contain at least the hinge, CH<sub>2</sub> and CH<sub>3</sub> domains of the constant region of an Ig heavy chain or the Fc portion of the heavy chain" and "the use of IgG-3 constant region in said fusion proteins." (*Id.*) The Patent Office then concluded that:

it would have been **prima facie obvious** to one of ordinary skill in the art at the time the invention was made to **have created the claimed invention** because Schall et al. teach the nucleic acid sequence encoding an insoluble (eg. membrane bound) 55kD TNF receptor while Capon et al. teach DNA encoding soluble Ig/ligand binding fusion proteins wherein the ligand binding protein is a soluble portion derived from a cell surface receptor. One of ordinary skill in the art **would have been motivated to do the aforementioned** because Capon et al. teach that the ligand binding portion of the Ig/ligand binding fusion protein can be derived from a wide variety of different known cell surface receptors and that said fusion proteins have a variety of uses. (*Id.*) (Citations omitted.)

It is respectfully submitted that the Patent Office has impermissibly used hindsight reconstruction to arrive at the claimed subject matter. Indeed, the rejection is based upon the Patent Office's conclusion that it would have been "*obvious to ... have*

*created the claimed invention.*" This is similar to the "could have" and "would have been able to" approaches that have been rejected by the Federal Circuit as being inappropriate yardsticks of patentability. See e.g., *Orthokinetics Inc. v. Safety Travel Chairs Inc.*, 1 USPQ2d 1081, 1087 (Fed. Cir. 1986) and *Ex parte Levengood*, 28 USPQ2d 1300, 1301-02 (BPAI 1993); see also *McGinley v. Franklin Sports, Inc.*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001).

Specific use of hindsight is shown by the Patent Office's focus upon Capon at "column 10, second paragraph." By basing the rejection upon that selected portion of Capon, the Patent Office overlooked the *preceding* paragraph at column 10, the first sentence of which states:

Ordinarily, the ligand binding partner is fused C-terminally to the N-terminus of the constant region of immunoglobulins in place of the variable region(s) thereof, however N-terminal fusions of the binding partner are also desirable.

Read in context, the above sentence suggests replacing *only* the variable region(s) of an immunoglobulin molecule. In other words, the *entirety* of the constant region(s) is left *intact*. That is not what is recited in the rejected claims, however. Claims 66 and 67 recite a DNA encoding "the extracellular domain of a TNF receptor polypeptide ... functionally attached to a Fc portion and hinge region of an IgG heavy chain polypeptide" and the remaining claims recite a DNA subsequence that "encodes all of the domains, other than the first domain, of the constant region of the heavy chain of a human immunoglobulin."

Thus, Capon's suggestion of what one should "ordinarily" do leads away from the claimed subject matter. This is evidence of nonobviousness.

To be fair, the second paragraph at column 10 relied upon the Patent Office is relevant. However, it must be read in context with the preceding paragraph, and with all of the relevant disclosure of the second paragraph, which states:

Typically, such fusions retain at least functionally active hinge, CH<sub>2</sub> and CH<sub>3</sub> domains of the constant region of an immunoglobulin heavy chain. Fusions are also made to the C-terminus of the Fc

portion of a constant domain, or immediately N-terminal to the CH1 of the heavy chain or the corresponding region of the light chain....

The first sentence quoted above is consistent with the first full paragraph at column 10 to the extent it specifies that "at least" the mentioned parts of the constant region are retained. In other words, "at least" the mentioned parts of the constant region embraces the entirety of the constant region. And each of the two alternatives suggested in the second sentence quoted above are outside the scope of the claims.

The Patent Office has offered no reason or explanation as to why one of ordinary skill would have ignored and proceeded contrary to the first full paragraph at column 10 of Capon. Likewise, no reason or explanation has been offered to explain why one of ordinary skill would have ignored and proceeded contrary to the second sentence of the second paragraph. There is simply no basis or reason, other than the impermissible use of hindsight, to selectively focus upon and narrowly interpret the first sentence of the second paragraph.

It is well settled that all portions of a prior art reference must be considered for what they fairly teach. *In re Rinehart*, 189 USPQ 143, 146-47 (CCPA 1976) ("A determination under 35 USC 103, however, requires consideration of the entirety of the disclosure made by the two references to those skilled in the art.") It is legal and factual error for the PTO to selectively rely upon only so much of a cited reference that supports the PTO's rejection, while ignoring the remainder of the reference. *In re Wesslau*, 147 USPQ 391, 393 (CCPA 1965) ("It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.")

Schall does not describe or suggest a fusion protein of any kind. Therefore, Schall offers nothing to suggest employing a soluble portion of a human TNF binding protein in a fusion protein, nor the DNA encoding such a fusion protein. The Examiner has pointed to nothing in Capon or Schall which would provide motivation to

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select a soluble portion of an insoluble TNF binding protein and integrate a DNA encoding the same into a fusion construct in the manner recited in the claims.

It is respectfully submitted that the rejection is factually and legally insufficient and should be withdrawn.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejections and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

No fee, other than the \$750.00 fee for filing under Rule 129 and the \$414.00 fee for the additional claims is due. If any fee is deemed necessary, the Commissioner is hereby authorized to charge payment of any additional fees associated with this communication or credit any overpayment to Deposit Account No. 08-2525..

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